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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,903	11/15/2005	Takashi Hirao	1254-0298PUS1	7071
	7590	EXAMINER		
PO BOX 747			BERTAGNA, ANGELA MARIE	
FALLS CHURCH, VA 22040-0747			ART UNIT	PAPER NUMBER
			1637	
			NOTIFICATION DATE	DELIVERY MODE
			12/29/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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	Application No.	Applicant(s)			
	10/556,903	HIRAO ET AL.			
Office Action Summary	Examiner	Art Unit			
	ANGELA BERTAGNA	1637			
The MAILING DATE of this communication app Period for Reply	pears on the cover sheet with the c	orrespondence address			
A SHORTENED STATUTORY PERIOD FOR REPLY WHICHEVER IS LONGER, FROM THE MAILING DA - Extensions of time may be available under the provisions of 37 CFR 1.13 after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period w - Failure to reply within the set or extended period for reply will, by statute, Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION 36(a). In no event, however, may a reply be tim vill apply and will expire SIX (6) MONTHS from a cause the application to become ABANDONE	lely filed the mailing date of this communication. (35 U.S.C. § 133).			
Status					
Responsive to communication(s) filed on <u>22 At</u> This action is FINAL . 2b)⊠ This Since this application is in condition for allowar closed in accordance with the practice under E	action is non-final. nce except for formal matters, pro				
Disposition of Claims					
4) Claim(s) 1-28 is/are pending in the application. 4a) Of the above claim(s) 9-28 is/are withdrawr 5) Claim(s) is/are allowed. 6) Claim(s) 1-8 is/are rejected. 7) Claim(s) is/are objected to. 8) Claim(s) are subject to restriction and/or Application Papers 9) The specification is objected to by the Examine 10) The drawing(s) filed on 15 November 2005 is/a Applicant may not request that any objection to the Replacement drawing sheet(s) including the correct	n from consideration. r election requirement. r. re: a)⊠ accepted or b)□ objected or bin o	e 37 CFR 1.85(a). ected to. See 37 CFR 1.121(d).			
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.					
Priority under 35 U.S.C. § 119 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) All b) Some * c) None of: 1. Certified copies of the priority documents have been received. 2. Certified copies of the priority documents have been received in Application No 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). * See the attached detailed Office action for a list of the certified copies not received.					
Attachment(s) 1) Notice of References Cited (PTO-892) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date See Continuation Sheet	4) Interview Summary Paper No(s)/Mail Da 5) Notice of Informal P 6) Other:	ite			

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :11/15/05; 12/23/05; 7/18/06; 6/15/07; 11/16/07.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-8, in the reply filed on August 22, 2008 is acknowledged. The traversal is on the ground(s) that search and examination of all of the claims together would not present a significant examination burden. This argument was not persuasive, because the instant application is a national stage application filed under 35 U.S.C. 371. As a result, it is subject to the unity of invention standard, which does not require a showing of undue burden. It is noted, however, that search and examination of all of the claims together would present an undue burden, because the different inventions would require different and non-overlapping search strategies, particularly with regard to the different nucleic acid sequences recited in the claims. This additional search and analysis would impose an undue burden on the Examiner and the PTO search resources.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 22, 2008.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Application/Control Number: 10/556,903 Page 3

Art Unit: 1637

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

3. Applicant's submission of an Information Disclosure Statement on November 15, 2005, December 23, 2005, July 18, 2006, June 15, 2007, and November 16, 2007 is acknowledged. Signed copies are enclosed.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The hyperlinks appear on pages 1, 2, 19, and 20.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- 6. Claims 1-3 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Terry et al. (European Food Research and Technology (2001) 213: 425-431).

The instant claims are drawn to methods of quantifying a plant belonging to a specific plant genus in a food ingredient or food sample comprising quantitative PCR.

Regarding claim 1, Terry teaches a method of quantifying a plant belonging to a specific plant genus in a food or a food ingredient by a PCR method, comprising:

- (a) preparing a sample for correction, wherein a sample derived from the specific plant genus to be detected and a standard plant sample are mixed in a predetermined ratio, and extracting genomic DNA from the sample for correction (see page 426, "Soybean samples" and "Sample DNA extraction and purification" sections, where DNA is isolated from the 0%, 0.1%, 1%, and 2% (w/w) mixtures of soya flour/Roundup Ready soya flour);
- (b) preparing a test sample where a known amount of the standard plant sample is added to the food or the food ingredient to be examined, and extracting genomic DNA from the test sample (see page 426, "Soybean samples" and "Sample DNA extraction and purification" sections, where DNA is isolated from the previously used mixture of soya flour/Roundup Ready soya);
- (c) practicing a quantitative PCR using a primer set for detecting the sample derived from the specific plant genus to be detected and a primer set for detecting the standard plant sample with the genomic DNA extracted from each of the sample for correction and the test sample as a template (page 426, column 2 page 427, column 1);
- (d) determining, as a standard value for correction, a value of the copy number of the DNA derived from the standard plant/the copy number of the DNA derived from the specific plant genus for the sample for correction by the quantitative PCR method (see pages 426-427, pages 429-430, Figures 1-3 and Tables 7-9); and

(e) determining a value of the copy number of the DNA derived from the specific plant genus/the copy number of the DNA derived from the standard plant for the test sample by the quantitative PCR method, and correcting the value with the standard value for correction to calculate the amount of the plant belonging to the specific plant genus contained in the food or the food ingredient (see pages 426-427, pages 429-430, Figures 1-3 and Tables 7-9).

Regarding claims 2 and 3, Terry teaches real-time quantitative PCR using TaqMan probes (see pages 426-427).

Regarding claim 6, the Roundup Ready soya detected by Terry is a member of the *Glycine* genus.

Claim Rejections - 35 USC § 103

- 7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

Application/Control Number: 10/556,903

Art Unit: 1637

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Terry et al. (European Food Research and Technology (2001) 213: 425-431) in view of Hirao et al. (US 2003/0207298 A1).

Claim 8 is drawn to the method of claim 2, wherein the specific plant genus to be detected is *Fagopyrum* and primers of SEQ ID NO: 14 and 15 are used in combination with a probe of SEQ ID NO: 64 to practice the quantitative PCR method.

Terry teaches the methods of claims 1-3 and 6, as discussed above.

Terry does not teach that the specific plant genus to be detected is *Fagopyrum*.

Hirao teaches PCR-based methods for detecting a target plant genus in a food ingredient (see abstract, paragraph 5, and paragraphs 13-15).

Regarding claim 8, Hirao teaches detecting the plant genus *Fagopyrum* via PCR (see Examples 1-2 on pages 6-14). Hirao also teaches that the instant SEQ ID NO: 14 and SEQ ID NO: 15 are useful primers for the specific amplification of the *Fagopyrum* genus (paragraphs 40 and 189-190). Hirao also teaches that the complement of the instant SEQ ID NO: 64 (*i.e.* SEQ ID NO: 12) is a useful primer for the specific amplification of the *Fagopyrum* genus (paragraph 40). Hirao further teaches that the *Fagopyrum* plant genus is allergenic (paragraphs 5-7).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to apply the method of Terry to the detection of the plant genus

Fagopyrum. An ordinary artisan would have been motivated to apply the method of

Page 7

Art Unit: 1637

Terry to the detection of any clinically relevant plant genus, such as the allergenic *Fagopyrum* genus taught by Hirao. An ordinary artisan would have had a reasonable expectation of success in applying the method of Terry to the detection of the *Fagopyrum* genus, since Hirao taught that the claimed oligonucleotides or their complements were useful for the specific amplification of the *Fagopyrum* genus. Thus, the method of claim 8 is *prima facie* obvious over Terry in view of Hirao.

9. Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terry et al. (European Food Research and Technology (2001) 213: 425-431) in view of Palacios et al. (Molecular Phylogenetics and Evolution (2000) 14(2): 232-249; cited on an IDS).

Claims 4 and 5 are drawn to the method of claim 1, wherein the standard plant belongs to a plant species other than upland weeds and food crops, specifically statice.

Terry teaches the method of claims 1-3 and 6, as discussed above.

Terry does not teach that the standard plant is statice.

Palacios analyzed the nuclear ITS sequences from the Limonium (statice) genus by RFLP and PCR amplification followed by sequencing (pages 233-237).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to use statice as the standard plant when practicing the method of Terry. An ordinary artisan would have been motivated to use any readily available plant, such as the statice taught by Palacios, when practicing the method of Terry, recognizing that the choice of the standard was not critical to practice of the invention provided that DNA could be extracted and amplified therefrom. In other words, the ordinary artisan would

Page 8

Art Unit: 1637

have recognized that the statice plant samples taught by Palacios and the non-genetically modified soya flour used by Terry were equivalents useful for the same purpose, and therefore, would have been motivated to substitute one for the other with a reasonable expectation of success. As noted in MPEP 2144.06, it is *prima facie* obvious to substitute equivalents known to be useful for the same purpose in the absence of unexpected results. Also, as noted in MPEP 2144.07, it is *prima facie* obvious to select a known material based on its suitability for the intended purpose in the absence of unexpected results. Thus, the methods of claims 4 and 5 are *prima facie* obvious over Terry in view of Palacios.

10. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Terry et al. (European Food Research and Technology (2001) 213: 425-431) in view of Palacios et al. (Molecular Phylogenetics and Evolution (2000) 14(2): 232-249; cited on an IDS) and further in view of GenBank Accession Number (AJ222860; December 2000) and further in view of Buck et al. (BioTechniques (1999) 27: 528-536).

Claim 7 is drawn to the method of claim 2, wherein the standard plant is statice, wherein SEQ ID NO: 57-58 are used as a primer pair in the quantitative PCR method, and wherein SEQ ID NO: 59 is used as a probe in the quantitative PCR method.

Terry teaches the method of claims 1-3 and 6, as discussed above.

Terry does not teach that the standard plant is statice.

Palacios analyzed the nuclear ITS sequences from the Limonium (statice) genus by RFLP and PCR amplification followed by sequencing (pages 233-237).

Application/Control Number: 10/556,903

Art Unit: 1637

Palacios does not teach using the claimed oligonucleotides as amplification primers or probes.

GenBank Accession Number AJ222860 teaches the partial sequence of the 18S and 26S rRNA genes, ITS1, and ITS2 of *Limonium sinuatum*, which is a statice. The instantly claimed sequences are contained in this nucleic acid (see alignments below).

SEQ ID NO: 57

SEQ ID NO: 58

SEQ ID NO: 59

Buck analyzed the effect of primer design strategy on the performance of DNA sequencing primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that every single primer worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned

when repeated. Further, every single control primer functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to use statice as the standard plant when practicing the method of Terry. An ordinary artisan would have been motivated to use any readily available plant, such as the statice taught by Palacios, when practicing the method of Terry, recognizing that the choice of the standard was not critical to practice of the invention provided that DNA could be extracted and amplified therefrom. In other words, the ordinary artisan would have recognized that the statice plant samples taught by Palacios and the non-genetically modified soya flour used by Terry were equivalents useful for the same purpose, and therefore, would have been motivated to substitute one for the other with a reasonable expectation of success. As noted in MPEP 2144.06, it is *prima facie* obvious to substitute equivalents known to be useful for the same purpose in the absence of unexpected results. Also, as noted in MPEP 2144.07, it is *prima facie* obvious to select a known material based on its suitability for the intended purpose in the absence of unexpected results.

It also would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to design amplification primers and probes based on any stretch of sequence contained in GenBank Accession Number AJ222860 (for example, the claimed SEQ ID NO: 57-59) in order to amplify and detect statice using the quantitative PCR method suggested by the teachings of Terry and Palacios. Since Buck clearly demonstrated the equivalence of primer sequences, the ordinary biochemist would have anticipated a reasonable level of success in using any amplification primers and probes in the method resulting from the combined teachings of Terry and Palacios. Therefore, absent any secondary considerations, the use of the claimed oligonucleotides in the method resulting from the combined teachings of Terry and Palacios is *prima facie* obvious in light of the teachings of GenBank Accession No. AJ222860 and Buck.

Attention is also directed to *KSR Int'l Co. v. Teleflex Inc.* (550 U.S._____, 127 S. Ct. 1727 (2007)) where the Supreme Court determined that "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103 (*KSR*, 550 U.S. at _____, 82 USPQ2d at 1397)."

In this case, as discussed above, the sequence of the 18S and 26S rRNA genes, ITS1 and ITS2 regions of the statice plant *Limonium sinuatum* was well known in the art as demonstrated by GenBank Accession No. AJ222860. This prior art would have suggested to the ordinary artisan a finite number of possible oligonucleotide primers and probes. An ordinary artisan would have expected predictable results, and thus would

have had a reasonable expectation of success, in pursuing this finite number of possible oligonucleotides suggested by the prior art of GenBank Accession No. AJ222860, since oligonucleotide synthesis methods were well known in the art at the time of invention and also since Buck clearly demonstrated the equivalence of primer sequences. Thus, the method of claim 7 is *prima facie* obvious over the cited references in the absence of secondary considerations.

11. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Terry et al. (European Food Research and Technology (2001) 213: 425-431) in view of Nair et al. (Fagopyrum (1999) 16: 29-36; cited on an IDS) and further in view of Yasui et al. (Genes & Genetic Systems (1998) 73: 201-210) and further in view of Buck et al. (BioTechniques (1999) 27: 528-536).

Claim 8 is drawn to the method of claim 2, wherein the specific plant genus to be detected is *Fagopyrum*, wherein SEQ ID NO: 14-15 are used as a primer pair in the quantitative PCR method, and wherein SEQ ID NO: 64 is used as a probe in the quantitative PCR method.

Terry teaches the method of claims 1-3 and 6, as discussed above.

Terry does not teach that the specific plant genus to be detected is *Fagopyrum*.

Nair teaches that buckwheat (*Fagopyrum esculentum*) is allergenic (page 29) and analyzed the nucleic acid encoding the major allergenic protein by RT-PCR and DNA sequencing (pages 29-30).

Yasui analyzed the ITS sequences of several *Fagopyrum* species (see abstract and pages 201-203) and deposited the DNA sequences in GenBank as GenBank Accession

Numbers AB000322 - AB000342 (see abstract and pages 201-203). The instantly claimed oligonucleotides are contained in GenBank Accession Number AB000334 from *Fagopyrum leptopodum* (see Figure 2 of Yasui and the alignments below).

```
SEQ ID NO: 14
Qу
         1 CGCCAAGGACCACGAACAGAAG 22
           Db
       119 CGCCAAGGACCACGAACAGAAG 140
SEQ ID NO: 15
         1 CGTTGCCGAGAGTCGTTCTGTTT 23
Qу
           Db
       219 CGTTGCCGAGAGTCGTTCTGTTT 197
SEQ ID NO: 64
         1 CGGGACGCGCTTC 13
QУ
           Db
        149 CGGGACGCGCTTC 137
```

Buck analyzed the effect of primer design strategy on the performance of DNA sequencing primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that every single primer worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, every single control primer functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were

surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to apply the method of Terry to the detection of the plant genus Fagopyrum. An ordinary artisan would have been motivated to apply the method of Terry to the detection of any clinically relevant plant genus, such as the allergenic Fagopyrum genus taught by Nair. In applying the method of Terry to the detection of the Fagopyrum genus, an ordinary artisan would have been motivated to design amplification primers and probes based on any stretch of sequence contained in GenBank Accession Number AB000334 taught by Yasui (for example, the claimed SEQ ID NO: 14, 15, and 64) in order to amplify and detect *Fagopyrum* using the quantitative PCR method suggested by the teachings of Terry and Nair. Since Buck clearly demonstrated the equivalence of primer sequences, the ordinary biochemist would have anticipated a reasonable level of success in using any amplification primers and probes in the method resulting from the combined teachings of Terry and Nair. Therefore, absent any secondary considerations, the use of the claimed oligonucleotides in the method resulting from the combined teachings of Terry and Nair is *prima facie* obvious in light of the teachings of Yasui and Buck.

Attention is also directed to *KSR Int'l Co. v. Teleflex Inc.* (550 U.S._____, 127 S. Ct. 1727 (2007)) where the Supreme Court determined that "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103 (*KSR*, 550 U.S. at _____, 82 USPQ2d at 1397)."

In this case, as discussed above, the sequence of the ITS region of the several Fagopyrum species were known in the art as demonstrated by Yasui. This prior art would have suggested to the ordinary artisan a finite number of possible oligonucleotide primers and probes for detection of Fagopyrum. An ordinary artisan would have expected predictable results, and thus would have had a reasonable expectation of success, in pursuing this finite number of possible oligonucleotides suggested by the prior art of Yasui, since oligonucleotide synthesis methods were well known in the art at the time of invention and also since Buck clearly demonstrated the equivalence of primer sequences. Thus, the method of claim 8 is prima facie obvious over the cited references in the absence of secondary considerations.

Conclusion

12. No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 9-5.

Application/Control Number: 10/556,903 Page 16

Art Unit: 1637

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/ Primary Examiner, Art Unit 1637

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